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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,087	11/20/2001	Stephen G. Sligar	87-00	1280
23713	7590	12/30/2004	EXAMINER	
GREENLEE WINNER AND SULLIVAN P C			LI, RUIXIANG	
4875 PEARL EAST CIRCLE			ART UNIT	
SUITE 200			PAPER NUMBER	
BOULDER, CO 80301			1646	

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	09/990,087		SLIGAR ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Ruixiang Li		1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 37,39-49 and 51-59 is/are pending in the application.
- 4a) Of the above claim(s) 44-49 and 51-58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 37 and 39-43 is/are rejected.
- 7) ☐ Claim(s) 59 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### **Applicants' Amendment, Claims, and Status of Application**

Applicants' amendment filed on 08/25/2004 and Supplemental Response filed on 10/12/2004 have been entered in full. Claims 38, 50, and 60 have been canceled. Claims 37, 40, 42-45, 47, 49, 51, 53, 54, 56, and 59 have been amended. Claims 37, 39-49, and 51-59 are pending. Claims 37, 39-43, and 59 are under consideration, whereas claims 44-49 and 51-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Applicants' request to rejoin nonelected species is noted. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

### **Withdrawn Rejections and/or Objections**

The rejection of claims 59 and 60 under 35 U.S.C. §112, second paragraph, as set forth at page 3 of the Office action (05022004, mailed on 05/11/2004), has been withdrawn in view of amended and canceled claims.

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The rejection of claims 37 and 59 under 35 U.S.C. §102 (b) as being anticipated by Bayburt et al. (*Journal of Structural Biology* 123:37-44, 1998), as set forth at page 5 in the previous office action (Paper No. 8, June 11, 2003), has been withdrawn in view of amended claims and Applicants' argument.

**Claim Rejections under 35 USC § 112, 1<sup>st</sup> paragraph (Scope of Enablement)**

(i) The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii) Claims 37, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nanoscale particle comprising G-protein coupled receptor, does not reasonably provide enablement for a nanoscale particle comprising an integral membrane protein with a seven transmembrane segment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the

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claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The claims recite a nanoscale particle comprising an artificial membrane scaffold protein and at least one integral membrane protein, wherein said protein is a seven transmembrane segment protein. Thus, the claims encompass not only a G-protein coupled receptor, but also an integral membrane protein with a seven transmembrane segment that is not coupled with a G protein (Ji et al., G protein-coupled receptors. 273:17299-17302, 1998; see, in particular, 3<sup>rd</sup> paragraph of left column of page 17299). While the specification provides sufficient guidance on how to make and use a nanoscale particle to reconstitute a G-protein coupled receptor, and how to make a nanoscale particle comprising an integral membrane protein with a seven transmembrane segment, the specification fails to teach how to use a nanoscale particle comprising an integral membrane protein with a seven transmembrane segment because the biological function of such a protein is not disclosed in the instant disclosure. Neither the biological functions of such a protein are taught in the prior art. One skill in the art would have to determine the biological functions of such a protein. Thus, it would require undue experimentation for one skilled in the art to make and use the invention commensurate in scope with these claims.

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Accordingly, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

### **Claim Rejections Under 35 U. S. C. § 112, 2<sup>nd</sup> Paragraph**

Claims 37 and 39-43 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 recite "wherein said protein" (line 10)". It is unclear whether the term refers to "scaffold protein" or "integral membrane protein" recited earlier in the claim, rendering the claims indefinite. Claims 39-43 are rejected as dependent claims.

### **Claim Rejections under 35 USC § 103 (a)**

Claims 37 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bayburt et al. (*Journal of Structural Biology* 123:37-44, 1998) in view of Barnes et al. (*Neuropharmacology* 38:1083-1152, 1999).

Bayburt et al. teach reconstitution and imaging of an integral membrane protein, NADPH-cytochrome P450 reductase in a nanometer-size phospholipid bilayer. This nanobilayer consists of an approximately 10-nm-diameter circular (discoidal) phospholipid domain stabilized by apolipoprotein A1, an amphipathic membrane scaffold protein (See, e.g., Abstract), which forms  $\alpha$ -helices (top of right column of page

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37). The apolipoprotein A1 has eight 22-mer and two 11-mer tandem amino acid sequence repeats, each with the periodicity of an amphipathic  $\alpha$  helix.

Bayburt et al. fail to teach a nanoscale particle comprising a G-protein coupled receptor, such as a 5-hydroxytryptamine receptor.

Barnes et al. teach the structures and biological functions of 5-hydroxytryptamine receptors. Barnes et al. teach a high level of interest in the actions of 5-hydroxytryptamine and that pharmacological manipulation of the central 5-hydroxytryptamine system has therapeutical potential (see, e.g., Abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to reconstitute a 5-hydroxytryptamine receptor of Barnes et al. in the nanometer-size phospholipid bilayer taught by Bayburt et al. with a reasonable expectation of success. One would have been motivated to do so because (i) the nanometer-size phospholipid bilayer provides a novel approach for the study of mechanical and functional properties of single-membrane proteins in a bilayer environment, which represents a physiologically relevant condition, as taught by Bayburt et al (see, e.g., Abstract; 2<sup>nd</sup> paragraph of left column of page 38; last paragraph of left column of page 44); and (ii) pharmacological manipulation of the central 5-hydroxytryptamine system has therapeutical potential (see, e.g., Abstract), as taught by Barnes et al.

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### **Claim Objections**

Claims 42 and 59 are objected to because they recite unelected subject matter, amino acid sequences (SEQ ID NOS: 6, 9, 19, 23, 29, 43-45).

It is also suggested that "wherein said protein" (line 6 of claim 59) be amended to "wherein said membrane scaffold protein" for consistence and clarity.

Appropriate correction is required.

### **Conclusion**

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875.

The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For



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more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.



Ruixiang Li, Ph.D.  
Examiner  
December 27, 2004